Progress in Biophysics and Molecular Biology 122 (2016) 16–23

Contents lists available at ScienceDirect

Progress in Biophysics and Molecular Biology

journal homepage: www.elsevier.com/locate/pbiomolbio

The biological default state of cell proliferation with variation and motility, a fundamental principle for a theory of organisms

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ARTICLE INFO

Article history:
Received 3 March 2016
Received in revised form
24 June 2016
Accepted 26 June 2016
Available online 2 July 2016

Keywords:
Default state
Theory
Organicism
Emergence
Mathematical symmetries
Biological organization

ABSTRACT

The principle of inertia is central to the modern scientific revolution. By postulating this principle Galileo at once identified a pertinent physical observable (momentum) and a conservation law (momentum conservation). He then could scientifically analyze what modifies inertial movement: gravitation and friction. Inertia, the default state in mechanics, represented a major theoretical commitment: there is no need to explain uniform rectilinear motion, rather, there is a need to explain departures from it. By analogy, we propose a biological default state of proliferation with variation and motility. From this theoretical commitment, what requires explanation is proliferative quiescence, lack of variation, lack of movement. That proliferation is the default state is axiomatic for biologists studying unicellular organisms. Moreover, it is implied in Darwin's "descent with modification". Although a "default state" is a theoretical construct and a limit case that does not need to be instantiated, conditions that closely resemble unrestrained cell proliferation are readily obtained experimentally. We will illustrate theoretical and experimental consequences of applying and of ignoring this principle.

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http://dx.doi.org/10.1016/j.pbiomolbio.2016.06.006
0079-6107/

"… we should supplement Virchow's well-known tenet of the cell theory: 'Omnis cellula e cellula,' by its counterpart: 'Omnis organisatio ex organisatione.' If the former denies spontaneous generation of living matter, the latter denies spontaneous generation of organization. In admitting this, we merely paraphrase what Whitman has called the "continuity of organization." But within these specified limits the cell, even in development, is still, as Schwann has said, an individual."

Weiss, P. (1940). The problem of cell individuality in development. The American Naturalist, 74:34–46.

1. Introduction

Biologists and philosophers have long pondered the differences between inert matter and living entities. Rather than concentrating on this type of comparison, we will mention some compelling characteristics of the living that should be taken into consideration when addressing biological phenomena. They are: agency (the capacity to initiate action[1]), normativity (the capacity of generating their own rules), individuation (the ability to change one's own organization), the propensity to become sick, and the return to health. In this regard, Bichat referring to physical deformities stated: "Whereas monsters are still living beings, there is no distinction between normal and pathological in physics and mechanics".[2] The distinction between the normal and the pathological holds for living beings alone". Inspired by Canguilhem, we will add that the opposite of pathological is not "normal" but "healthy" (Canguilhem, 1991). This is illustrated by the fact that individuals experiencing *situs inversus totalis* (heart in the right side, liver in the left side) may be perfectly healthy without being normal.

There are differences between the inert and the alive, and thus between the sciences that study them (Longo and Soto, 2016). In this regard, it is pointless to try to fit biology into physics, as one would when thinking that because a prebiotic world preceded the advent of life, life would represent a particular case of the physical "world". In fact, scientists do not directly deal with the "real world" but with scientific disciplines constructed by the human mind to understand such a world. Hence, when we refer to the physical or biological, we are referring to the disciplines that address inert and living matter, respectively. Thus, we can only talk about the coherence between the two disciplines. That is, living matter "obeys" the laws of physics, but additional principles and observables may be necessary to understand organisms. When biology is interpreted as "extended physics" the inert state of matter can be considered as a special case or a singularity of the living state of matter. In this case, physics is biology when all organisms are ignored or dead. In science, similar conceptual transitions already exist: after Riemann, Euclidian Geometry instead of being considered the ultimate foundation of mathematics has been viewed as a special case, a singularity: Riemann's geometry on space of no curvature (that is, curvature 0).

Before the 20th century, biologists often explicitly stated the philosophical bases for their observations, experiments and theories. Two examples of this practice are Blumenbach's correspondence with Kant about a "formative force" (Lenoir, 1982) and Darwin's explicit mention of being influenced by Whewell (Ruse, 1975). In the preceding articles of this issue we have addressed the role of theory on the choice of the observables and the construction of objectivity, particularly the founding role of Galileo's inertia in classical mechanics. This principle represents a limit case: if no cause (a force) modifies the properties of an object, the object conserves its properties. In the rigorous mathematical sense, this is a limit or asymptotic case since there are always frictions and gravitational forces and no physical body can be exactly identified to a point-mass moving on a Euclidean straight line. For didactic purposes we use the term "default state" (borrowed from computer science) to denote a state that applies when "no action is taken". In short, the default state is what happens when nothing is done to the intended object or system in question. Galileo's choice of inertia as a fundamental theoretical postulate was counter-intuitive because objects present in our immediate surroundings are subject to forces that hinder the manifestation of such a state. The counter-intuitiveness of Galilean inertia is illustrated by the fact that Kepler and Leibnitz thought that the opposite was true, namely, that "The globe [meaning a planet] has a natural inertia or stillness, for which it remains at rest in every place, where it is posed alone [quoted in: Bussotti, (2015)].

The crucial point is that accepting inertia as a postulate implies that *we do not need to explain uniform rectilinear motion*, *rather*, *we need to explain departures from it*. The usefulness of this postulate remains uncontested in classical mechanics. In fact, 300 years after Galileo, this counter-intuitive postulate was buttressed by E Noether's theorems; they provided a deeper understanding of inertia by justifying conservation properties of energy and momentum on the basis of time and space symmetries, respectively (van Fraassen, 1989). Ever since, symmetries (and their breaking) acquired an even more fundamental role in physics.

In short, the conservation of these symmetries is based on the idea that the 'laws' of physics are the same at different positions and times. In spite of the advance due to Noether's theorem, the notion of symmetries is already used in Archimedes' law of the lever: equal weights at equal distances are in equilibrium. This article proposes a biological default state which would play a comparable useful role in organismal biology.

2. Existing biological theories

Biology has one comprehensive theory, the theory of evolution which encompasses the time-scale of phylogenesis and is based on two principles, i) reproduction with modification, and ii) natural

[1] These definitions of agency, normativity and individuality are chosen because they are brief and broadly useful. They have been discussed more extensively (Burge, 2009; Moreno and Mossio, 2015) and Miquel and Hwang, 2016).
[2] Quoted by (Canguilhem, 2008) page 90.